

Serial No. 10/089,220  
 PCT Appl. Filed: September 29, 2000  
 Page 2 of 11

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

1. (currently amended) A process for sensing a biological or chemical change changes in molecular conformation ~~structural shape~~ or mass of a biomolecule molecules attached to the surface of a transverse shear piezoelectric oscillating molecular sensing device driven by a network analyser, said change being attributable to a binding interaction between said biomolecule attached to the surface and a biological entity in a surrounding liquid medium upon exposure of the surface to the surrounding liquid medium, said process comprising the steps of:

i) exciting said sensing sensor device at a series of predetermined frequencies prior to and during exposure to the surrounding liquid medium;

ii) collecting data from the sensing device to determine values for ~~the~~ predetermined parameters: series resonance frequency shift ( $f_s$ ), motional resistance ( $R_m$ ) ( $RM$ ), motional inductance ( $L_m$ ) ( $LM$ ), motional capacitance ( $C_m$ ) ( $CM$ ), electrostatic capacitance ( $C_o$ ), and boundary layer slip parameter ( $\alpha$ );

iii) determining a relative change in said measured parameters in step ii) upon exposure of the surface to the surrounding liquid medium; and to detect thereby any changes in molecular structural shape or mass at sensing device surface.

iv) correlating the relative change in said parameters determined in step iii) with a calibrated set of data for said parameters to determine a change in molecular conformation or mass of the biomolecule attached to the surface attributable to a binding interaction upon exposure to the surrounding liquid medium;

wherein a change in boundary layer slip parameter ( $\alpha$ ) and an essentially zero change in the series resonance frequency shift ( $f_s$ ) confirms a change in molecular conformation and essentially zero change in mass of the biomolecule attached to the surface.

2. (canceled)

3. (canceled)

4. (canceled)

Serial No. 10/089,220  
PCT Appl. Filed: September 29, 2000  
Page 3 of 11

5. (currently amended) The process according to claim 1 wherein said biomolecule attached to the surface is ~~entities bound to the sensor are~~ selected from the group consisting of proteins and nucleic acids.
6. (original) The process according to claim 5 wherein said proteins are selected from the group consisting of antibodies, enzymes, molecular receptors, receptor ligands and polypeptides.
7. (original) The process according to claim 5 wherein said nucleic acids are selected from the group consisting of DNA, RNA and oligonucleotides.
8. (currently amended) The process according to claim 1 wherein said biological entity molecules in liquid in said surrounding liquid medium is are selected from the group consisting of proteins and nucleic acids.
9. (original) The process according to claim 8 wherein said proteins are selected from the group consisting of antibodies, enzymes, molecular receptors, receptor ligands and polypeptides.
10. (original) The process according to claim 8 wherein said nucleic acids are selected from the group consisting of DNA, RNA and oligonucleotides.
11. (canceled)
12. (canceled)
13. (canceled)

Response for 10/089,220 (PAT 457W-2)  
Allowed Claims 1 to 4 of  
European Application EP 00963840.4  
Page 1

**Claims 1 to 4 as Allowed in Europe**

1. A process for sensing a chemical change in molecular conformation or mass of a biomolecule attached to the surface of a transverse shear piezoelectric sensing device driven by a network analyser, said change being attributable to a binding interaction between said biomolecule attached to the surface and a biological entity in a surrounding liquid medium upon exposure of the surface to the surrounding liquid medium, said process comprising the steps of:

- i) exciting said sensing device at a series of predetermined frequencies prior to and during exposure to the surrounding liquid medium;
- ii) collecting data from the sensing device to determine values for the following parameters: series resonance frequency shift ( $f_s$ ), motional resistance ( $R_m$ ), motional inductance ( $L_m$ ), motional capacitance ( $C_m$ ), electrostatic capacitance ( $C_o$ ), and boundary layer slip parameter ( $\alpha$ );
- iii) determining a relative change in said parameters in step ii) upon exposure of the surface to the surrounding liquid medium; and
- iv) correlating the relative change in said parameters determined in step iii) with a calibrated set of data for said parameters to determine a change in molecular conformation or mass of the biomolecule attached to the surface attributable to a binding interaction upon exposure to the surrounding liquid medium.

2. The process according to claim 1 wherein a change in boundary layer slip parameter ( $\alpha$ ) and an essentially zero change in series resonance frequency shift ( $f_s$ ) confirms a change in molecular conformation and essentially zero change in mass of the biomolecule attached to the surface.

Response for 10/089,220 (PAT 457W-2)  
Allowed Claims 1 to 4 of  
European Application EP 00963840.4  
Page 2

3. The process according to claim 1 or 2 wherein said biomolecule attached to the surface is selected from the group consisting of:  
proteins, such as antibodies, enzymes, molecular receptors, receptor ligands or polypeptides; and  
nucleic acids such as DNA, RNA or oligonucleotides.
4. The process according to any one of claims 1 to 3 wherein said biological entity in the surrounding liquid medium is selected from the group consisting of:  
proteins, such as antibodies, enzymes, molecular receptors, receptor ligands or polypeptides; and  
nucleic acids, such as DNA, RNA or oligonucleotides,  
said biological entity being capable of a binding interaction with the molecule attached to the surface.